PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
IRVINE, Jonquil Claire
J.A. KEMP & CO.
14 South Square
Gray's Inn
London WC1R 5LX
GRANDE BRETAGNE

Fax 44 207 242 8932

J.A. KEMP & Co.
Rec'd. 24 DEC 2001
Action by.....

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing *(day/month/year)*	14.12.2001
Applicant's or agent's file reference: N.77933A JCI	**REPLY DUE** **within 1 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/03760	02/10/2000	01/10/1999

International Patent Classification (IPC) or both national classification and IPC
G01N33/68

Applicant
ISIS INNOVATION LIMITED et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☒	Lack of unity of invention
V	☐	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain document cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 01/02/2002.

Name and mailing address of the international preliminary examining authority:
European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer / Examiner
GONCALVES M L F C

Formalities officer (incl. extension of time limits)
Danti, B
Telephone No. +49 89 2399 8161

I. Basis of the opinion

1. With regard to the **elements** of the international application (Replacement *sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*):

Description, pages:

1-58 as originally filed

Claims, No.:

1-59 as originally filed

Drawings, sheets:

1/39-39/39 as received on 04/12/2000 with letter of 04/12/2000

Sequence listing part of the description, pages:

1-20, filed with the letter of 20.11.2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1-38 and 40-59 (part); 39,

because:

   ☒ the said international application, or the said claims Nos. 40, 41, 42 relate to the following subject matter which does not require an international preliminary examination (*specify*):
   see separate sheet

   ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-38 and 44-59 (part); 39 are so unclear that no meaningful opinion could be formed (*specify*):
   see separate sheet

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos. .

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation (Form PCT/IPEA/405) to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

☒ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with for the following reasons and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees:

3. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this opinion:

☒ all parts.

☐ the parts relating to claims Nos. .

Section III

1. In view of the large number and also the wording of the claims presently on file, which render it difficult, if not impossible, to determine the matter for which protection is sought, the present application fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful complete examination is impossible (see also section V, items I.2, II.1 and III.1).

2. The application comprises claims defining the invention in terms of the result to be achieved (example claim 39) which do not comply with the requirements of Article 6 PCT. The scope of claim 39 is not defined, thus examination is not possible.

3. The application comprises claims to methods of diagnostic practised on the human or animal body, as well as claims to methods of treatment practised on the human or body (example claims 40, 41 and 42). For the assessment of such claims on the question whether they are industrially applicable, no unified criteria exists in the PCT. The patentability can also be dependent upon the formulation of the claims.

Section IV

1. The claims currently on file relate to three different inventions:

   I) Celiac disease diagnostic methods, agents and kits: independent claims 1, 2, 13, 14, 15, 16, 17 , 21, 22, 25, 26, 27, 28, 38, 40, 41, 42, and the claims dependent thereon;

   II) Plant cells, plants and parts of plants that express mutant gliadin proteins, foods and crops containing such plants: independent claims 31, 35, 46, 47, 48, 49, 51, 52, 53, 54, 55, 57, 58 and the claims dependent thereon;

   III) Polynucleotides encoding mutant gliadin, cells transformed with

Polynucleotides encoding mutant gliadin, transgenic animals and antibodies against mutant gliadin: independent claims 12, 19, 20, 29, 30, 31, 37 and the claims dependent thereon.

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons: The sequence of a natural occurring homologue of gliadin or its analogue (that is the technical feature common to the abovementioned groups of claims) is already known from documents D1 to D4. The requisite unity of invention (Rule 13.1 PCT) therefore no longer exists inasmuch as a technical relationship involving one or more of the same or corresponding special technical features in the sense of Rule 13.2 PCT does not exist between the subject-matter of the abovementioned groups of independent claims.

The applicant has paid the fees relative to the examination of the aforementioned three inventions.

Section V

Invention I:

Celiac disease diagnostic methods, agents and kits: independent claims 1, 2, 13, 14, 15, 16, 17 , 21, 22, 25, 26, 27, 28, 38, 40, 41, 42, and the claims dependent thereon.

I.1 The wording of claim 1 is such that the subject-matter of the claim is very broad, and consequently lacks novelty regarding the disclosures in the following documents cited in the search report (Article 33(2) PCT).

D1: O'KEEFFE J ET AL: "T cell proliferation, MHC class II restriction and cytokine products of gliadin-stimulated peripheral blood mononuclear cells (PBMC)." CLINICAL AND EXPERIMENTAL IMMUNOLOGY, vol. 117, no. 2, August 1999 (1999-08), pages 269-276, XP000989621 ISSN: 0009-9104

D2: VAN DE WAL YVONNE ET AL: "Small intestinal T cells of celiac disease patients recognize a natural pepsin fragment of gliadin." PROCEEDINGS OF THE

NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 95, no. 17, 18 August 1998 (1998-08-18), pages 10050-10054, XP000982626 Aug. 18, 1998 ISSN: 0027-8424

D3: TRONCONE R ET AL: "Cytokines produced by gliadin-specific T cell clones from the coeliac mucosa." GASTROENTEROLOGY, vol. 110, no. 4 SUPPL., April 1996 (1996-04), page A1031 XP000989625 96th Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week;San Francisco, California, USA; May 19-22, 1996 ISSN: 0016-5085

D4: GODKIN A J ET AL: "Identification of a coeliac disease-specific T cell epitope from A-gliadin." GUT, vol. 44, no. SUPPL. 1, April 1999 (1999-04), page A72 XP000989626 British Society of Gastroenterology Annual Meeting;Glasgow, Scotland, UK; March 23-25, 1999 ISSN: 0017-5749

I.2 The remaining dependent and independent claims of invention I appear to relate to obvious alternatives of the method of claim 1 and are therefore not inventive (Article 33(3) PCT).

I.3 The Invention I contains a total of 19 claims, of which 17 are independent claims. In view of the large number and also the wording of the claims, which render it difficult, if not impossible, to determine the matter for which protection is sought, the present invention fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful complete examination is impossible.

Invention II:

Plant cells, plants and parts of plants that express mutant gliadin proteins, foods and crops containing such plants: independent claims 35, 46, 47, 48, 49, 51, 52, 53, 54, 55, 57, 58 and the claims dependent thereon.

II.1 The subject-matter of claim 35, a cell comprising a mutant gliadin protein epitope, is anticipated by the disclosure in the following prior art document (Article 33(2) PCT):

D5: EP 0 905 518 A (UNIV LEIDEN ;ACADEMISCH ZIEKENHUIS LEIDEN

(NL)) 31 March 1999 (1999-03-31) .

II.2 The remaining dependent and independent claims of invention II (Plant cells, plants and parts of plants that express mutant gliadin proteins, foods and crops containing such plants) appear to relate to obvious alternatives to the subject-matter of claim 35 and are therefore not based on an inventive concept (Article 33(3) PCT).

II.3 The Invention II contains a total of 14 claims, of which 13 are independent claims. In view of the large number and also the wording of the claims, which render it difficult, if not impossible, to determine the matter for which protection is sought, the present invention fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful complete examination is impossible.

Invention III:

Polynucleotides encoding mutant gliadin, cells transformed with Polynucleotides encoding mutant gliadin, transgenic animals and antibodies against mutant gliadin: independent claims 12, 19, 20, 29, 30, 31, 37 and the claims dependent thereon.

III.1 The subject-matter of claim 12 lacks novelty regarding the disclosures in the following documents cited in the search report (Article 33(2) PCT).

D1: O'KEEFFE J ET AL: "T cell proliferation, MHC class II restriction and cytokine products of gliadin-stimulated peripheral blood mononuclear cells (PBMC)." CLINICAL AND EXPERIMENTAL IMMUNOLOGY, vol. 117, no. 2, August 1999 (1999-08), pages 269-276, XP000989621 ISSN: 0009-9104

D2: VAN DE WAL YVONNE ET AL: "Small intestinal T cells of celiac disease patients recognize a natural pepsin fragment of gliadin." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 95, no. 17, 18 August 1998 (1998-08-18), pages 10050-10054, XP000982626 Aug. 18, 1998 ISSN: 0027-8424

D3: TRONCONE R ET AL: "Cytokines produced by gliadin-specific T cell clones from the coeliac mucosa." GASTROENTEROLOGY, vol. 110, no. 4

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D4: GODKIN A J ET AL: "Identification of a coeliac disease-specific T cell epitope from A-gliadin." GUT, vol. 44, no. SUPPL. 1, April 1999 (1999-04), page A72 XP000989626 British Society of Gastroenterology Annual Meeting;Glasgow, Scotland, UK; March 23-25, 1999 ISSN: 0017-5749

D5: EP 0 905 518 A (UNIV LEIDEN ;ACADEMISCH ZIEKENHUIS LEIDEN (NL)) 31 March 1999 (1999-03-31) .

III.2 The remaining dependent and independent claims of invention III (Polynucleotides encoding mutant gliadin, cells transformed with Polynucleotides encoding mutant gliadin, transgenic animals and antibodies against mutant gliadin) appear to relate to obvious alternatives to the subject-matter of claim 12 and are therefore not based on an inventive concept (Article 33(3) PCT).

III.3 The Invention III contains a total of 10 claims, of which 7 are independent claims. In view of the large number and also the wording of the claims, which render it difficult, if not impossible, to determine the matter for which protection is sought, the present invention fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful complete examination is impossible.